

1. A method for identifying at least one binder molecule comprising the steps of:
 (a) choosing two amino acid types (AA1 and AA2) in a polypeptide or protein of interest, whereby AA2 at least once occurs directly subsequent to AA1 in the amino acid sequence of the polypeptide or protein, defining an amino acid pair AA1-AA2;

5 (b) labeling the two amino acid types (AA1 and AA2) in the polypeptide or protein of interest, whereby all AA1-residues is labeled with ^{13}C and all AA2-residues with ^{15}N ;

10 (c) generating a first HNCO-type NMR spectrum of the labeled polypeptide or protein from step (b), thereby identifying signals from the labeled amino acid pair AA1-AA2;

(d) contacting the labeled polypeptide or protein with a potential binder molecule or a mixture of binder molecules under conditions and sufficient time for allowing binding of the potential binder molecule or the binder molecules and the labeled polypeptide or protein;

15 (e) generating a second HNCO-type NMR spectrum, or a ^1H - ^{15}N correlation type NMR spectrum, of the mix from step (d), monitoring signals identified in step (c); and

(f) comparing the first and the second NMR spectra, whereby a chemical shift change of the signals identified in step (c) between the two spectra indicates an interaction between the potential binder molecule and the labeled polypeptide or protein.

20 2. The method of claim 1, wherein the labeled amino acid pair AA1-AA2 is unique within a sphere radius of 10 Å within the polypeptide or protein.

25 3. The method of claim 1, wherein the labeled amino acid pair AA1-AA2 is unique within a sphere radius of 50 Å within the polypeptide or protein.

4. The method of claim 1, wherein the labeled amino acid pair AA1-AA2 is unique within the polypeptide or protein.

5. The method of claim 1, wherein the labeled amino acid pair AA1-AA2 is within a binding pocket of the polypeptide or protein.

6. The method of claim 1, wherein the labeled amino acid pair AA1-AA2 is in the proximity of an active site within the polypeptide or protein.

7. The method of claim 1, wherein the result of the method is compared to the result of any other suitable binding or activity assay.

8. The method of claim 1, wherein the polypeptide or protein has a size of from 10 to 150 kDa.

9. The method of claim 1, wherein the potential binder molecule is a peptide, polypeptide, protein, antibody, nucleic acid molecule, or carbohydrate.

10. The method of claim 1, wherein the potential binder molecule comprises a complex of one or more of a peptide, polypeptide, protein, antibody, nucleic acid molecule, or carbohydrate.

11. The method of claim 1, wherein the potential binder molecule has a molecular mass of from 50 to 1000 Da.

12. The method of claim 1, wherein the method is used for screening a compound library.